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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KOLKER, DANIEL E

ART UNIT PAPER NUMBER

1649

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/035,977		DESNOYERS ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Daniel Kolker		1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 6/13/05, 7/1/05.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22 - 30, 32 - 35, and 38 - 41 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22 - 30, 32 - 35, and 38 - 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>6/13/05</u> .   | 6) <input type="checkbox"/> Other: _____                                    |

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### **DETAILED ACTION**

1. Applicant's remarks, amendments, and declarations filed 13 June and 1 July 2005 have been entered. Claims 31, 36, and 37 have been cancelled; claims 22 – 30, 32 – 35, and 38 – 41 are pending and under examination.
2. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The deletion of inventors under 37 CFR 1.48(b) is accepted.

### ***Information Disclosure Statement***

5. The information disclosure statement filed 13 June 2005 has been considered. The BLAST results indicate that applicants are aware of nucleic acids and proteins with relevant to examination. However the results cannot be considered because there is no alignment provided, nor is there an indication of the percent identity between the claimed sequence and the reference sequences. Applicant states on p. 9 of the remarks that the newly-submitted documents include references to specific accession numbers and sequences. Applicant is advised that the BLAST results submitted appear to be the results of a search and include a list of sequences which match, but do not provide either alignments or indications of how the sequences are related to the instantly-claimed peptides. Therefore the examiner cannot determine if the sequence accession numbers submitted by applicant constitute prior art. Furthermore the search results submitted appear to be the results of a search and are not publicly available documents. Applicant is directed to MPEP 609 and 37 CFR and 1.98 (a) – (d).

### ***Withdrawn Objections and Rejections***

6. The following objections or rejections made in the previous office action are withdrawn:  
The objections to the specification. Applicant has deleted the hyperlinks and changed the title.

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The rejection of claims 22 – 27 and 34 – 35 under 35 USC 112, first paragraph, for lacking enablement as far as it relates to deposit of biological material. Applicant's declaration filed 13 June 2005 is sufficient to overcome the rejection.

The rejections under 35 USC 112, second paragraph. Applicant's amendments are sufficient to overcome the rejections.

### ***Rejections Maintained***

#### ***Priority***

7. In the previous office action the examiner determined that the effective filing date for this application is the date the international application was filed, 1 March 2000. Applicant did not traverse this determination and thus it stands for the reasons made of record.

#### ***Claim Rejections - 35 USC §§ 101 and 112***

8. Claims 22 – 30, 32 – 35, and 38 – 41 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The rejection is maintained for the reasons made of record in the previous office action and reiterated below.

The claims are drawn to isolated nucleic acids encoding polypeptides, called PRO4380, as well as variants at least 80% identical thereto fragments of same, as well as nucleic acids which comprise same and vectors and host cells. The specification asserts that PRO4380 has two specific utilities, as it came up positive in two assays, however neither utility is substantial.

Applicant did not address the examiner's arguments that the first assay, (Example 37, page 166), which discloses compounds that test positive as either stimulators or inhibitors of glucose or FFA uptake, does not constitute a patentable utility. This assay is deemed to lack utility for the reasons made of record in the previous office action, p. 4 second complete paragraph – p. 5, first complete paragraph).

The data presented in Example 41 (p. 168 – 169) of the specification indicate that PRO4380 was positive in the Mouse Kidney Mesangial Cell Proliferation Assay. It is acknowledged that proliferation of mammalian kidney mesangial cells is useful as Schocklmann (1999. Kidney International 56:1199-1207) teaches that such proliferation is necessary after injury or damage to the kidney. However, the threshold used in determining whether a

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particular PRO molecule counts as “positive” in this assay would not be considered reasonable by one of skill in the art. The specification discloses (p. 169, lines 1 – 2) that positives in this assay include anything which is at least 15% over the control reading. The post-filing publication by Rovin et al. (2002. *Kidney International* 61:1293-1302) indicates that a 21% increase in human mesangial cell proliferation is not statistically significant (see particularly p. 1296, lines 3 – 6).

On page 10 of the remarks applicant refers to the utility guidelines on specific, substantial, and credible utilities. The claims were not rejected for lack of credible utility, thus arguments related to this point (i.e page 10, point (3) in the final paragraph) are not germane. Particularly, the citation of MPEP 2107 II (B)(1)(ii), drawn to credible utilities is not on point as no rejection for lack of credibility was made.

On p. 11 of the remarks, applicant argues that utility need not be proven, that a reasonable correlation between the evidence and the asserted utility is sufficient, and that the asserted utility should be accepted if it is more likely than not true. Applicant cites *In re Langer*, *In re Jolles*, *In re Irons*, *In re Sichert*, *Raytheon v. Roper*, and *In re Oetiker* as supporting this argument. Applicant’s arguments have been fully considered but are not persuasive.

In *In re Langer*, the court ruled the Patent Office cannot require clinical testing in humans to rebut a prima facie case for lack of utility. In the instant case, the Office has not made such a requirement. Furthermore the Langer court ruled that “Assuming that sufficient reason to question the statement of utility and its scope does exist, a rejection for lack of utility under § 101 will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the statement of utility and its scope as found in the specification are true.” In the instant case there is in fact sufficient reason to question the statement of utility. The reference by Rovin cited in the previous office action indicates that the 15% threshold used by applicant is not reasonable. Therefore one of skill in the art would have reason to doubt the asserted utility.

In *In re Jolles*, the issue was whether data from an art-recognized animal model could be considered predictive of results in humans. That is not an issue in the instant case, as the examiner indicated in the paragraph spanning pp. 5 – 6 of the previous office action that proliferation of mammalian kidney mesangial cells would be useful, as it is an important part of the repair process after injury (see Schocklmann, particularly pp. 1199 - 1200 for more detailed discussion). But since the threshold used by applicant was 71% of a change shown not to be

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statistically significant, one of skill in the art would conclude that there PRO4380 does not induce any more mesangial cells than are induced under control conditions.

The citation of *In re Irons* is also not relevant to the instant case. In *Irons*, evidence was submitted that indicated that the drug had been administered to 888 patients and that statistically significant results were obtained showing an improvement in arthritic conditions. In the instant case, no such evidence has been submitted. In the instant case, the claimed product has not been administered to patients. Furthermore, there is no evidence of record indicating a statistically significant result *in vitro*.

The *Sichert* court ruled that blind comparative studies of the claimed compositions, which showed that the compositions were effective in relieving lymphatic congestion (as narrowly defined), were sufficient to establish utility of said compositions under 35 USC § 101. In the instant case, applicant has not shown any such studies, and therefore because the fact pattern is sufficiently different the *Sichert* case is not germane.

In *Raytheon v. Roper*, utility was found by the Federal Circuit when a lack of utility had been found by a lower court. This was due not to the sufficiency of the evidence presented, but rather because the Federal Circuit ruled that the claims in question had been interpreted erroneously. In the instant case, there does not appear to be a question as to how the pending claims are being interpreted.

It is not immediately apparent why applicant has cited *In re Oetiker* in arguments related to the utility under 35 USC § 101, as the *Oetiker* case dealt not with utility but with obviousness under 35 USC § 103. No claims have been rejected under § 103 in the instant case.

The examiner acknowledges that the ability to induce mesangial cell proliferation is specific. However, the assay used by applicant and reported in Example 41 beginning on p. 168 of the specification would not allow a skilled artisan to conclude that it is more likely than not that the asserted utility is true and therefore the asserted utility is not substantial.

On p. 12 of the remarks applicant discusses the examiner's interpretation of the results from Rovin. The examiner and applicant appear to agree on this point. Rovin clearly stated that the data point, a 21% increase, did not represent a significant difference due to the large degree of variability inherent in this assay. Because of the large degree of error, a 21% increase is not significant. Stated another way, one of skill in the art would recognize that it is *improper* to conclude that the two samples (control and 5 uM ciglitazone) are drawn from different populations.

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Significance does not mean, as applicant asserts on p. 12, final paragraph, of the remarks, that there is not an overlap of standard deviations or errors in the data set. Rather, statistical significance is a determination, based on mathematic procedures, that the observed difference between samples has a less than 5% chance of occurring by random accident (see attached definition from the On-line Medical Dictionary, accessed 22 July 2005). Applicant argues that Rovin's report of a 21% non-significant difference indicates that the statistical error in their measurement overlaps with the statistical error in the control set, and that "this does not mean that an increase of proliferation of 21% is not scientifically important or significant, but means that Rovin's particular measurement of 21% may be incorrect due to the amount of error for that data point." This is not the way significance is understood in the art. Significance is an inference. When a result reaches statistical significance, it is proper to infer that the two samples are drawn from separate populations. When the result is not significant, the appropriate inference is not that the particular value is subject to error, but rather that it is not possible to tell if the two samples were drawn from separate populations. Applicant is directed to the attached text from the chapter by Freund et al. (2003. Statistical Methods, Second Edition, pp. 117 – 138), particularly the definition of "significance level" on p. 126 and the definition of "p value" on p. 133 for a more complete understanding of the way statistics are used in scientific papers. In the instant case, Rovin et al. used analyses of variance, followed by post-hoc Bonferroni-corrected pairwise comparisons (see p. 1295, second column "Statistical Analysis") rather than the standard argued by applicant. The teachings of Rovin indicate that this assay has so much variability that even if a 21% difference is detected when 12 experimental and 12 control samples are provided (see legend for Figure 2 which indicates that "[e]ach point represents the mean of at least 3 individual experiments done in quadruplicate").

On p. 13 of the remarks, applicant points out that Rovin found an 18% increase was significant. Applicant again asserts his own definition of significance (p. 13, second complete paragraph) which contradicts that provided on p. 1295 of Rovin. It is noted that this level is still greater than the changes reported in the specification, where only a 15% increase is considered important. However, taken with the finding that a 21% increase in this assay is not significant, this finding further supports the examiner's point that knowing the variability associated with the measurements is crucial to determining whether or not the artisan will conclude that samples are drawn from different populations. In the instant case, the specification does not disclose the variability in the sample, so a skilled artisan would not reasonably conclude that PRO4380

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induces mesangial cell proliferation. The basis for questioning the utility of the instantly-claimed product provided herein is based on sound scientific analysis. While applicant's arguments have been considered they are not persuasive because no evidence has been provided to substantiate the assertion that the 15% change observed is an appropriate cutoff point. Thus the rejection under 35 USC § 101 stands.

9. Claims 22 – 30, 32 – 35, and 38 – 41 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Even if enablement were found for PRO4380, enablement would not be commensurate in scope with claims 22 – 30, 32 – 35, and 38 - 41, because the specification does not reasonably provide enablement for polynucleotides less than 100% identical to SEQ ID NO:56, or for polynucleotides less than 100% identical to those that encode SEQ ID NO:57, wherein the encoded polypeptides have the ability to induce mesangial cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant is directed to paragraph number 8 for a more complete discussion of why claims to SEQ ID NO:57 are not deemed to be able to induce mesangial cell proliferation. In summary, applicant has shown that in a single trial, SEQ ID NO:57 induced a 15% increase in the number of mesangial cells. Applicant did not disclose the variability in this system, and Rovin teaches that the variability in this assay is so high that even a 21% change, calculated as the difference between the average of 12 experimental and 12 control samples, is not significant. Freund teaches that it is not proper to conclude that samples are drawn from separate populations when the test statistic exceeds the significance level. In the instant case, the assay performed by Rovin appears to be identical to that performed by applicant. Both used mammalian mesangial kidney cells, and even used the same detection reagent from Promega. The teachings of Rovin indicate that knowing the variability level of the assay is crucial to making conclusions as to whether or not the differences are significant. Because applicant's results fall below both the lowest level shown by Rovin to be significant, and below a level shown by Rovin to be non-significant, a skilled artisan would not conclude that SEQ ID NO:57 increases mesangial cell proliferation in the absence of providing statistically significant results.



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Instead the artisan would conclude that the ability of SEQ ID NO:57 to induce proliferation is no different than that of a control.

On p. 14, third complete paragraph of the remarks applicant refers to pp. 109 – 111 of the specification as providing guidance as to how to make the claimed variants. However this text does not indicate which regions of PRO4380 (i.e. SEQ ID NO:57), or of the nucleic acids encoding PRO4380 (i.e. SEQ ID NO:56) are to be retained and which regions can be altered. Applicant also refers to p. 113, line 21 of the specification as teaching how to isolate DNA that encodes PRO polypeptides generally. However isolation of DNA is not at issue here, what is at issue is whether the specification provides an enabling disclosure of how to make and use nucleic acid variants commensurate in scope with the claims without resorting to undue experimentation. In this case, the artisan would have to undertake a large amount of experimentation and there is no guidance in the specification as to which regions of SEQ ID NO:56 must be retained. Applicant also argues that pp. 114 – 126 of the specification teach uses for PRO generally. It is noted that pp. 114 – 119 line 3 disclose how to select and transform host cells, how to select and use vectors, how to detect gene amplification, and how to purify polypeptides. None of these appear to be patentable utilities, since the claimed nucleic acid and encoded protein are not useful. Page 119 – 124 disclose uses of PRO that are not specific to the instantly-claimed molecule (i.e. use as hybridization probe to detect itself, as antisense to prevent its own expression, or in the construction of transgenic or knockout animals). Furthermore the utilities asserted on these pages are not germane to the scope of enablement rejection, as the relevant issue is whether the claims are enabled over their full scope, not whether there is any conceivable use for the nucleic acid.

11. Claims 22 – 26, 35, and 38 – 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant argues that the legal standard for the written description requirement is whether the disclosure “reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.” The examiner agrees with applicant’s definition. Applicant argues that the amendments to the claims, particularly the recitation “has the ability to induce mesangial cell proliferation” is sufficient to overcome the written description rejection.

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The examiner disagrees. The specification does not disclose any nucleic acids encoding polypeptide sequences at least 80, 85, 90, 95, or 99% identical to SEQ ID NO:57 which have the stated activity, with the sole exception of SEQ ID NO:56, the nucleic acid which encodes SEQ ID NO:57. The claims are drawn to genera of nucleic acids, but only a single member of the genus is disclosed. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention”. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”) Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a polypeptide, “requires a precise definition, such as by structure, formula, chemical name, or physical properties,” not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, “an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.” Id at 1170, 25 USPQ2d at 1606.” While the preceding quotation is drawn to DNA, the same logic applies to claims drawn to proteins and their variants.

Furthermore applicant has not shown which regions of the protein are important for the claimed activity. A description of a genus of proteins may be achieved by means of a recitation of a representative number of proteins, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated nucleic acid sequence SEQ ID NO:56 and a single polypeptide sequence SEQ ID NO:57. The additional limitation of requiring that the protein variants have the ability to

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induce mesangial cell proliferation fails to meet the written description requirement because it does not direct the artisan to those members of the claimed genera that meet the requirement. Furthermore the assay described has not been evidenced as providing either statistically or non-statistically related results that show conserved functions of the claimed members of the genera. Thus claims 22 – 26, 35, and 38 – 41 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

***Claim Rejections - 35 USC § 102***

12. Claims 22 – 27, 29, 35, and 38 – 41 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruben. The paragraph spanning pp. 13 – 14 of the previous office action indicate that Ruben teaches a sequence 95.3% identical to SEQ ID NO:56 as well as vectors and host cells comprising same. As set forth on p. 14 of the previous office action, the sequence from Ruben is identical to applicant's SEQ ID NO:56 from nucleotides 243 – 2134, including the entire region encoding PRO4380 without its signal peptide

On p. 17 of the remarks, applicant argues that the declaration of Goddard et al. is sufficient to overcome the rejections of claims 22 – 27, 29, 31, and 35 - 41. Applicant's arguments have been considered but are not persuasive. The declaration provides evidence that applicant was in possession of SEQ ID NO:56 and the protein encoded by it, SEQ ID NO:57, before the publication by Ruben. The declaration by Goddard et al. is not sufficient to overcome the rejection of claims 22 – 26 and 38 – 41. The declaration states that applicant was in possession of SEQ ID NO:56, but claims 22 – 26 are drawn to isolated nucleic acids at least 80, 85, 90, 95, or 99% identical to SEQ ID NO:56. The declaration does not provide evidence that applicant was in possession of any sequence less than 100% identical to SEQ ID NO:56 prior to the Ruben publication, nor does it provide evidence that applicant was in possession of a nucleic acid which hybridizes to SEQ ID NO:56 under the conditions recited in claim 35. Furthermore the declaration does not provide evidence that applicant was in possession of either SEQ ID NO:57 lacking its signal peptide or a nucleic acid encoding this fragment. These appear in claim 27, part (b) and claim 29. As stated in the previous office action, Ruben also teaches vectors and host cells which comprise the nucleic acid, and thus anticipates claims 38 – 41 as well.

***Rejections Necessitated by Amendment***

***Claim Rejections - 35 USC § 112***

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13. Claims 22 – 27, 30, 35, and 38 – 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims have been amended to recite “wherein the extracellular domain is amino acids 293 – 507”. There is no disclosure of this region being the extracellular domain. Figure 26 of the specification indicates the location of a transmembrane domain, but there is no disclosure of which end of the protein is intracellular and which end is extracellular. Since there was no disclosure of which regions were intracellular or extracellular in the specification, drawings, or claims as originally filed, identification of such regions is deemed to be new matter.

### ***New Rejections and Objections***

#### ***Oath/Declaration***

14. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration, particularly the changes to citizenship by Zhang and to address by Eaton. See 37 CFR 1.52(c).

#### ***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 22 – 27, 29, 30, 35, and 38 – 41 are rejected under 35 U.S.C. 102(e) as anticipated by (U.S. Patent application publication 2003/0100051, published 29 May 2003, filed

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10 September 2001, claiming priority to applications filed 28 June 2001, 10 November 1999, 6 May 1999, and claiming benefit of provisional applications filed 11 September 2000, 18 May 1998, and 12 May 1998).

Ruben et al. teach SEQ ID NOs:137, 139, and 242, each of which are 97.0% identical to applicant's SEQ ID NO:57 (see attached alignments). Ruben's sequences are identical to applicant's SEQ ID NO:57 from residues 16 – 507 (using applicant's residue numbers). Ruben also teaches that his invention includes isolated nucleic acids encoding each of the sequences, thereby meeting the limitations of claims 22 – 25, part (a) of each claim (see Ruben, Table 1 on pp. 94 – 97 for the identification of which nucleic acids encode which proteins). Applicant has identified residues 1 – 26 as the signal peptide (see Figure 26). Since the sequences from Ruben et al. are 100% identical to SEQ ID NO:57 starting at residue 16, the prior art sequence also meets the limitations of claims 27, 29, and 30, drawn to isolated nucleic acids encoding polypeptides comprising SEQ ID NO:57 lacking its associated signal sequence, independent of which end of the polypeptide is the extracellular domain. Similarly, the teachings of Ruben also anticipate claims 27, 30, and 35, which are drawn nucleic acids encoding polypeptides comprising the extracellular domain of SEQ ID NO:57. The prior art polypeptide sequence from Ruben is 100% identical to residues 16 – 507 of SEQ ID NO:57 (using applicant's residue numbers), and includes residues 293-507 which is identified as the extracellular domain in amended claim 22, for example. Since the polypeptides taught by Ruben are identical to those recited in claim 35, parts (b) and (c), the nucleic acids encoding them will inherently hybridize to applicant's nucleic acids under the recited conditions.

The claims, as amended, recite the functional limitation requiring that the polypeptide has the ability to induce mesangial cell proliferation; Ruben is silent as to this property. However, since the only differences between the prior art product and applicant's product is in the signal sequence which is cleaved off during protein processing, Ruben's polypeptides will inherently have the claimed properties. Ruben also teaches the nucleic acids in vectors, including those with sequences recognized by host cells (see Table 1 and pp. 120 - 121). Ruben teaches how to insert vectors into host cells and includes E. coli, yeast and CHO cells as preferred host cells (see p. 121, paragraphs 0830 – 0832).

It is acknowledged that applicant's declarations under 37 CFR 1.131 is sufficient to indicate that he was in possession of SEQ ID NO:56 prior to 18 November 1999. However the publication by Ruben cited herein claims benefit of provisional applications filed 12 May 1998

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and 18 May 1998. These are the same applications cited on the face of WO 99/58660, which was the basis of the rejection under 35 USC 102 (a) in the previous office action. Applicant is advised that the declarations filed both 13 June and 1 July 2005 have been considered, although it is not immediately obvious to the examiner how the two declarations differ, as they appear to be duplicates.

**Conclusion**

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.

September 12, 2005



SHARON TURNER, Ph.D.

PRIMARY EXAMINER

9-12-05